# BULLETIN

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## ON THE VALUE OF METHYLENE-BLUE IN MALARIAL FEVER.


By W. S. Thayer, *Resident Physician to the Johns Hopkins Hospital.*


Several months ago a report was made to the Medical Society of the Johns Hopkins Hospital[1] concerning some cases of malarial fever which were under treatment with methylene-blue, and the conclusion was reached, from what experience we had at that time, that methylene-blue had a distinct anti-malarial action and was possibly of some real value as an anti-malarial agent. It was then stated that a definite report would be made at a later date when increased experience might justify us in arriving at definite conclusions. These conclusions we now feel justified in expressing.

The first suggestion of the anti-malarial value of methylene-blue was made by Guttmann and Ehrlich.[2] These observers were led to undertake their experiments in consideration of the fact that methylene-blue stains the plasmodia not only in dried specimens but also in fresh blood, Celli and Guarnieri having stained the living plasmodia by mixing a drop of fresh blood with some slightly colored human blood serum; and also from the fact that certain elements in the red blood corpuscles, and particularly the nuclei of the nucleated red blood corpuscles in warm and cold-blooded animals, were also stained after the injection of methylene-blue into the circulation.

They observed two cases.

The first case was one of tertian ague, the chills occurring on the 21st, 23d, 25th and 27th of June. On the 28th of June methylene-blue 0.5 was given at 8 P. M. At 10.30 P. M. the patient complained of slight strangury. On the following day the temperature rose to 38.3° C., but there was no chill. After this the temperature remained normal. No malarial organisms were seen in the blood after July 1st, the third day, the patient having taken methylene-blue daily 0.1 five times in the 24 hours.

The second case was one of quotidian ague, daily chills occurring for three weeks. On the 18th of July at 3 P. M. methylene-blue 0.1 was given, to be repeated five times in the day. At 4 A. M. of the following day there was a chill lasting two hours, the temperature rising to 39° C. No chills or fever after this. On the 24th, six days later, the plasmodia had disappeared from the blood. They concluded that methylene-blue had a decided anti-malarial action, and they laid particular stress upon the importance of the discovery in view of the fact that none of the synthetical products, such as chinoline, kairin, antipyrin, antifebrin, ptyalin, phenacetine, etc., have ever had any effect on this disease. More recently Grawitz[1] has tried this drug in one case of chronic malarial intoxication without any marked effect.

In Professor Osler's wards in the Johns Hopkins Hospital seven cases of malarial fever have been systematically treated with methylene-blue.

[1] Johns Hopkins Hospital Bulletin, 1892, No. 19.
[2] Berliner Klinische Wochenschrift, 1891, No. 39.

[1] Berliner Klinische Wochenschrift, 1892, No. 9.

CASE 1. *Tertian ague; no fever 24 hours after administration of methylene-blue; disappearance of the organisms on the third day.* (*Temperature chart accompanying.*)

J. K., aged 58, a German by birth, was admitted to the Hospital on October 7th, 1891. Family history negative; previous history has no bearing on the present trouble. Has been living in a malarious district. Patient does not give a very clear history, but states that some time within the last two weeks he had three chills, after which he was given "medicine" which relieved him temporarily. Complains now of general weakness.

*Status Presens*, Oct. 8th. Large, well-formed man; lips and mucous membranes rather pale; respirations 16; pulse 48; temperature normal. Examination of thorax negative, barring a soft systolic souffle at the base of the heart; abdomen negative. Splenic dullness obliterated by abdominal tympany; border of the spleen not palpable. Legs were somewhat œdematous on entrance, but are now free from pitting. Large varicose veins on either leg.

*Urine* free from albumen or sugar.

*Blood.* Examination of one slide of blood showed no malarial organisms. The patient was given a nourishing diet and a bitter tonic, and after a day or two he was dressed and about the ward. On October 18th the patient had a slight chill, temperature rising to 102.2° at 4 P. M. By 8 o'clock at night the temperature was 98.4°. The fall in temperature was accompanied by sweating. On the 20th the patient had another chill, the temperature reaching 105° at 12 noon, the fall being accompanied again by profuse sweating. On the 21st examination of the blood showed numerous malarial organisms of the amœboid, intra-cellular variety, with fine, active pigment granules. At 8 P. M. methylene-blue 0.1 in capsules was given, to be repeated every three hours during the night, and to be continued five times in the twenty-four hours afterwards. On the following morning the temperature rose to 105° at 8 A. M., but there was no chill.

On the 23d there was a marked diminution in the number of organisms present.

On the 24th the temperature was normal and remained so afterwards. On this date the patient complained of burning with micturition and vesical tenesmus, which was relieved by a small amount of powdered nutmeg, about a quarter of a teaspoonful three times a day, as suggested by Guttmann and Ehrlich. On the 24th, the third day after the beginning of treatment, no organisms were found in the blood and the patient was discharged well on the second of November, repeated examinations having revealed no more organisms. This patient reported again at the Dispensary on the second of February, 1892. Had been perfectly well till a week or two before that date, when after being in a malarious district he had had a chill. He had taken quinine and at that time no organisms could be found.

CASE 2. *Chronic remittent fever with hyaline bodies and pigmented crescents in the blood. Fall of temperature to nearly normal point in 5 days, with marked diminution in the number of organisms. Irregular slight febrile attacks during the next month, with eventual increase in the number of organisms in the blood.*

*Entire disappearance of the fever in twenty-four hours under quinine, though occasional organisms were to be found in the blood twelve days later.* (*Temperature chart accompanying.*)

A. P., single, 20 years of age, admitted to the Hospital on the 24th of October. Family history good; personal history bears no relation to his present trouble. Present illness began 20 days ago with headache and general malaise and "creeping chills." These were relieved for a time by "medicine," but for the past few days he has been worse again.

*Status Presens.* Well-formed and nourished; lips and mucous membranes slightly pale; tongue thickly coated; skin warm and moist; pulse 84, dicrotic; general appearance typhoidal. Lungs and heart negative, excepting a soft systolic souffle in the pulmonary area. Abdomen not distended, splenic dullness (relative) begins at the eighth rib, border of the spleen easily palpable. No rose spots.

*Urine* free from albumen or sugar.

*Blood.* Numerous small, actively amœboid intra-corpuscular hyaline bodies. On the afternoon of the 25th of October methylene-blue 0.1 five times a day was ordered. The temperature fell during the next three days and on the 29th was perfectly normal. On the 30th the temperature touched 101.7°, and from the first to the 7th of November remained somewhat elevated, rising on the 3d as high as 103.5°. On the 2d of November the blood still contained a moderate number of hyaline bodies, also crescentic and ovoid bodies with coarse collections of pigment in the middle.

Nov. 3d methylene-blue 0.2 four times a day ordered. From the 7th to the 16th of November the temperature remained practically normal and the patient was out of bed and feeling much stronger. Occasional hyaline bodies, pigmented crescents and ovoid bodies were still, however, to be found. From the 16th to the 25th the temperature remained somewhat elevated, touching several times points about 101°, and the patient complained of headache and general malaise.

On the 21st, as the patient was rather anæmic, Fowler's solution, three minims three times a day, was ordered, to be increased one minim every third day, in addition to the methylene-blue. On the 25th, 26th and 27th the temperature remained nearly normal, but on the 28th it rose again to a point about 99.5°.

November 30th Fowler's solution omitted on account of slight conjunctivitis. On December 3d, as the patient had shown no improvement and the temperature had been rising for several days while the number of organisms in the blood was increasing, all medication was omitted and quinine gr. iv. three times a day was ordered. The temperature fell to normal on the 5th and remained so until his discharge on the 14th, eleven days after the beginning of treatment with quinine. In this time the patient had improved rapidly. The blood, however, still showed an occasional hyaline body and pigmented crescent. The patient was heard from by letter two weeks later. He stated that he felt perfectly well; he had been taking quinine.

In this case, after the first day or two of treatment there was slight burning with micturition which was relieved by a small amount of nutmeg with each dose of methylene-blue.

CASE 3. *Quotidian ague with pigmented intra-cellular organ-*

*isms, possibly of the tertian type, associated later with ovoid and crescentic bodies. One chill after the beginning of treatment; no rise above* 100° *after the fourth day. No organisms seen after the twelfth day. Patient discharged on the* 15*th day. Relapse a week after discharge.* (*Temperature chart accompanying.*)

Man, single, aged 17, admitted to the Hospital on the 27th of October. Family history good. Has had no previous illnesses. Present illness began 14 days ago with a chill followed by fever and sweating. This has been repeated every day, chills occurring at about ten in the morning.

*Status Presens.* Well-built, well nourished man, mucous membranes somewhat pale. Thorax negative; abdomen negative; spleen not palpable, though the splenic dullness begins at the upper border of the 8th rib and appears to pass the costo-articular line. *Urine* negative. *Blood* shows numerous large amœboid intra-cellular bodies with rather large pigment granules. The patient on admission was just recovering from a chill. On October 29th patient had a chill, the temperature rising to 104° at 12 noon. At 2 P. M. methylene-blue 0.1 five times a day was ordered. On October 30th patient had a chill, temperature reaching 103.2° at 12 noon.

October 31st, temperature rose to 103.4° at 12 noon, but there was no shaking. November 1st, temperature 100.1° at 2 P. M., no chill. November 2d, temperature 100.0° at 2 P. M. November 3d, temperature 99.6° at 12 noon. From that time on the temperature remained nearly normal, though it rose every day above 99°. On November 3d, five days after entrance, an occasional pigmented, crescentic body was seen, but none of the pigmented, intra-cellular bodies before observed. On the 7th of November, nine days after entrance, pigmented ovoid bodies and crescents and an occasional active hyaline body were found. On the 10th, twelve days after the beginning of treatment, no organisms were to be found, and from that time none were to be seen. On the 13th the patient was discharged with directions to continue treatment. In this case also there was slight strangury, which was relieved by nutmeg. This patient reported at the Dispensary on November 24th, stating that he had felt well up to three days before that time, eight days after discharge, when he began to lose appetite and have headache. Complained of thirst. Blood showed intra-cellular pigmented organisms. No careful search made. The patient was given quinine and has not reported since then.

The examinations of the blood in this case were not as thorough as they might have been, and it is quite possible that a more careful search might have revealed organisms even at the time of his discharge, as the early relapse would suggest. It is perfectly possible, however, that there was a new infection, as the district in which the patient lives is most malarious.

The case is of particular interest because of the presence of organisms apparently of the tertian type, together with the hyaline bodies and crescents which are usually associated with the more remittent and irregular forms of fever.

CASE 4. *Chronic malarial intoxication; no fever on entrance; vertigo and dizziness. Hyaline bodies and pigmented crescents in the blood. Rapid disappearance of the symptoms under methylene-blue; no organisms seen after the ninth day.*

J. S., married, aged 37, entered the Hospital on November 7th. Family history negative. Previous history has no bearing on his present trouble. Has been working on fishing boats on the bay since August. Complains now of weakness and a staggering gait. His present illness began six weeks ago with headache, malaise and fever, for which he took quinine pills.

*Status Presens.* Well-formed and nourished, lips and mucous membranes of good color, temperature normal, pulse slow and regular; thorax negative; abdomen negative except that the border of the spleen is easily palpable. *Urine* negative.

*Blood* showed ovoid and crescentic bodies with coarse, granular pigment in the middle, also an occasional small, actively amœboid intra-corpuscular hyaline body. On attempting to stand and walk the patient finds great difficulty in keeping his balance. After swaying to and fro for several moments he steadies himself and stands fairly well, but on any change of position loses his balance again. The knee jerks are slightly exaggerated; physical examination otherwise negative. On November 9th methylene-blue 0.2 four times a day was ordered. The temperature remained practically normal throughout his stay in the Hospital. On November 13th, six days after entrance, hyaline bodies were still to be found in the blood. On the 18th, nine days after the beginning of treatment, no organisms were seen. Dizziness disappeared within a few days after beginning of treatment. On November 27th the patient was discharged apparently well.

CASE 5. *Continued fever with irregular chills. Hyaline bodies and pigmented crescents present in the blood. Rapid fall of temperature to normal in four days with great diminution in the number of the organisms. No total disappearance of the organisms. Irregular febrile attack after a month's treatment, the number of organisms increasing. Marked improvement of general condition under quinine with disappearance of fever. Occasional organisms found in the blood at the date of discharge, two weeks after the beginning of treatment with quinine.* (*Temperature chart accompanying.*)

Man, single, 26 years of age, admitted to the Hospital on November 11th. Family history negative. Previous history has no bearing on his present trouble. Has been working at Sparrow's Point (a very malarious district) for one year. A month ago had an attack of tertian ague, took quinine and was benefited, but the chills never entirely ceased, though they became irregular. On the 10th of November had a severe chill. On the 11th was admitted with a chill, temperature reaching 104.8° at 3.30 P. M.

*Status Presens.* Well-formed and nourished, skin somewhat yellow in color, lips and mucous membranes rather pale; tongue thickly coated. Thorax negative. Spleen easily palpable. Abdomen otherwise negative. *Urine* negative.

*Blood* shows fairly numerous hyaline, actively amœboid organisms. Methylene-blue 0.1 every four hours was ordered at 8 P. M.

Nov. 12th, temperature touched 102.9° at 8 P. M.

Nov. 13th, temperature touched 103.4° at 4 P. M. Methylene increased to 0.2 four times a day.

Nov. 14th, temperature touched 100.6° at 6 P. M.

Nov. 17th: since the fifteenth the temperature has been normal. Blood to-day showed an occasional crescent.

November 24th: the temperature rose to-day to 101.4° at 6 P. M. and at midnight was 101.5°, patient complaining of headache.

November 26th: the temperature has remained more or less elevated. The blood, which has shown for ten days previously only an occasional crescent, now shows numerous hyaline, actively amœboid bodies. Fowler's solution, ℥iij three times a day, ordered, to be increased ℥i every third day. The temperature remained somewhat elevated until December 1st; from December 1st it was normal until the 7th, when it rose again to about 99.5° and the patient complained much of headache. Organisms were still present in the blood. Methylene-blue discontinued. Fowler's solution also discontinued on account of diarrhœa.

December 11th. The temperature rose at 4 P. M. to 100.7°. Quinine, four grains three times a day, ordered. On the 21st of December the temperature rose to 102.5° at 4 P. M., owing probably to a slight tonsillitis. On the 22d an occasional ovoid body was found in the blood and an occasional organism was still found when the patient was discharged on the first of January. The improvement in the general condition of the patient after quinine was begun was very marked. In the week from the 17th to the 26th the patient gained nine pounds and a half.

Case 6. *Quartan ague with pigmented, intra-cellular organisms; pigment rather large and not actively motile; organisms apparently not so large as those in ordinary tertian fever. No fever after the beginning of treatment. No organisms seen after the 9th day. Death from influenza and broncho-pneumonia one week after the omission of treatment by methylene-blue. No traces of blue found in the organs.* (*Temperature chart accompanying.*)

H. R., single, 52 years of age, admitted to the Hospital on the 10th of December. Family history negative. Previous history good. The present illness began on the 8th of December, when he had a severe chill, lasting for about an hour, followed by fever and sweating. Had none yesterday nor to-day.

*Status Presens.* Well-formed, rather sparely nourished, moderate muscular development. Lips and mucous membranes of good color; tongue slightly coated. Chest is somewhat barrel-shaped and rather hyper-resonant. Respiration clear throughout. Heart negative; spleen easily palpable; abdomen otherwise negative.

*Urine* negative. *Blood* showed fairly numerous round and ovoid, coarsely pigmented, intra-cellular bodies not quite filling the corpuscle. In some no motion at all could be made out. The pigment granules appeared coarser than those in the ordinary tertian form of the organism and of a slightly different color. No hyaline bodies, no crescents. On the 11th the patient had a chill, the temperature reaching 103.8° at 8 P. M. No segmenting bodies were seen, though a very careful search was not made. The fully developed organisms seen on this date did not seem to be as large as those seen in the ordinary tertian fever. The pigment granules seemed possibly larger and were not as motile. On the 14th the patient had another chill, the temperature rising to 104.3° at 6 P. M. On the 15th methylene-blue 0.1 four times a day was ordered, and from this date until the 30th of December there was no rise of temperature. On the 15th and 16th several plasmodia were found. On the 18th after a long search one pigmented organism was found. On the 22d, seven days after the beginning of treatment, careful examination of five slides showed no organisms. On the 1st of January the temperature, which had been slightly elevated on the two previous days, rose to 101.4°, and at 4 P. M. on the 2d touched 104.4°. The patient complained chiefly of headache. He had a cough with a muco-purulent expectoration. He was dull and listless. Repeated examinations of the blood on the 3d of January and on previous days had shown no organisms. Methylene-blue omitted. Dullness was made out at the right base, with somewhat enfeebled respiration and occasional fine râles. From this time until the patient's death on the 9th of January the temperature remained between 99.6° and 104°. The signs of bronchitis with areas of consolidation developed more markedly at the right base.

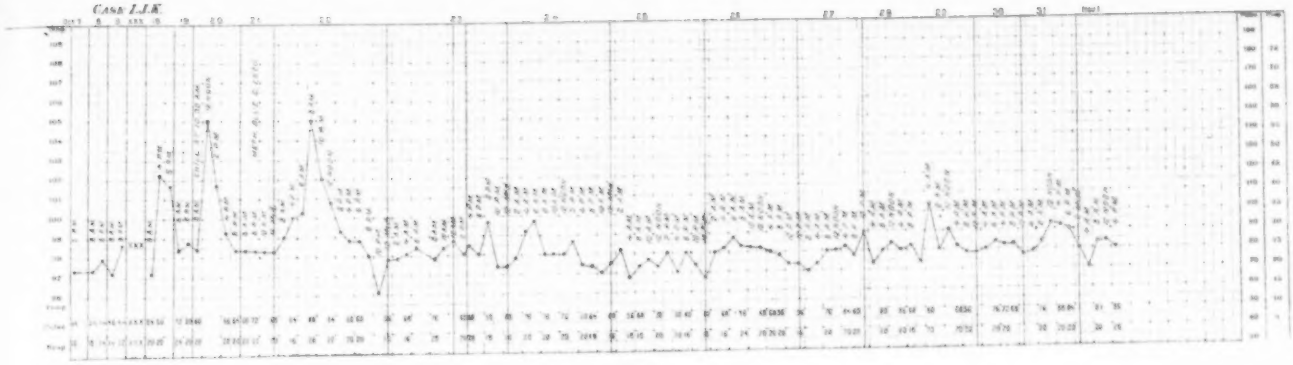
The autopsy, made on January 9th, showed a considerable degree of chronic interstitial pneumonia with old gummata in both lungs, particularly the right. In the right lower lobe numerous patches of broncho-pneumonia. Chronic interstitial orchitis; splenic tumor. No traces of methylene-blue could be found in any of the organs, though death occurred only six days after its omission.

Case 7. *Quotidian ague with organisms of the tertian type, probably a double tertian infection. Entire disappearance of fever after the 3d day with a great diminution in the numbers of organisms. Recurrence of the chills twenty two days after the last appearance of the fever, with increase in the number of organisms. Immediate disappearance of the fever with total disappearance of the organisms under quinine.* (*Temperature chart accompanying.*)

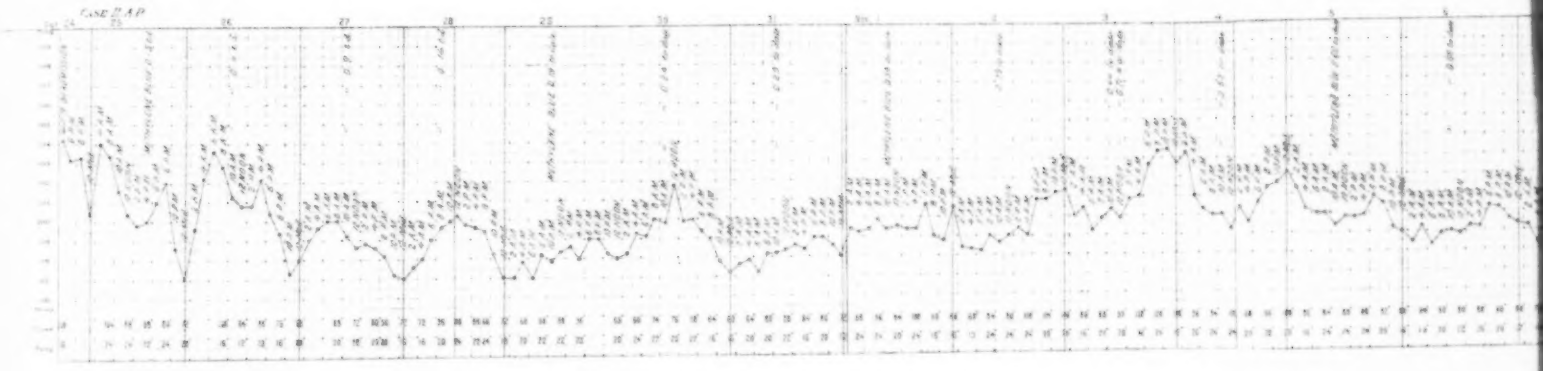
C. M., single, 33 years of age. Patient is a Pole and speaks no English or German, so that little history can be obtained. Has been working recently in a very malarious district. For the past seven months has had repeated attacks of chills and fever, which have been temporarily controlled by quinine. The chills were at first definitely tertian in type, but later became more irregular, and of late, according to the patient, have been quotidian. The patient was admitted just as he was recovering from a chill on January 8th. Temperature 102.2°, pulse 124, respirations 22. At 4 P. M. the temperature reached 104.8°.

*Status Presens.* Large frame, well-nourished; lips and mucous membranes slightly pale, tongue somewhat coated. Thorax negative; spleen easily palpable; abdomen otherwise negative. At 4 P. M. on the 9th the patient began to have another chill, the temperature reaching 101.8° at 6 P. M. At 2.30 P. M. on that day the blood showed numerous actively amœboid, intra-cellular bodies, filling up about half of a cell body and containing small active pigment granules. There was also a number of fully grown organisms with active pigment granules, some of which were beginning to show signs of segmentation. At the height of the chill numerous segmenting bodies with 15 to 20 segments were found, and towards the end of the chill small, hyaline, intra-cellular bodies began to appear. At 6 P. M. methylene-blue 0.2 every four hours was ordered. On the following day this was reduced to five doses in the 24 hours.

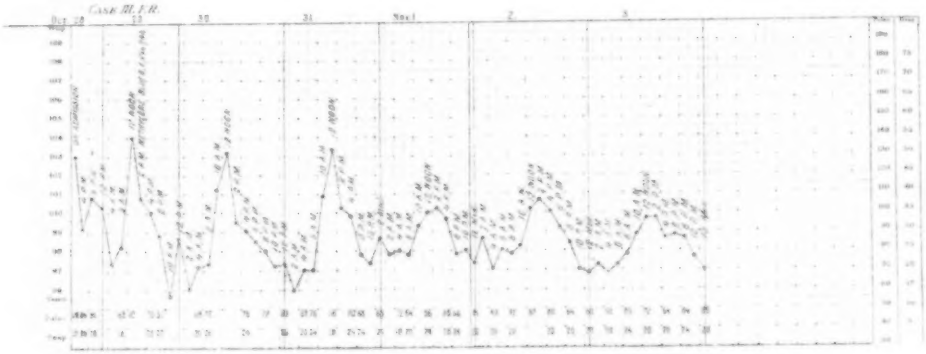
CASE I.J.K.



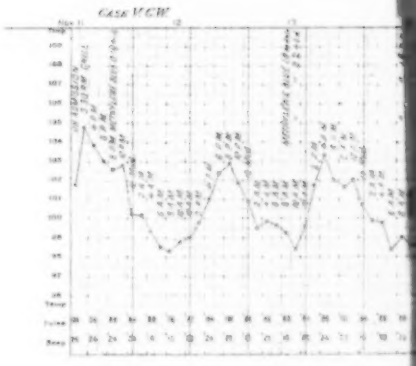
CASE II.A.P.



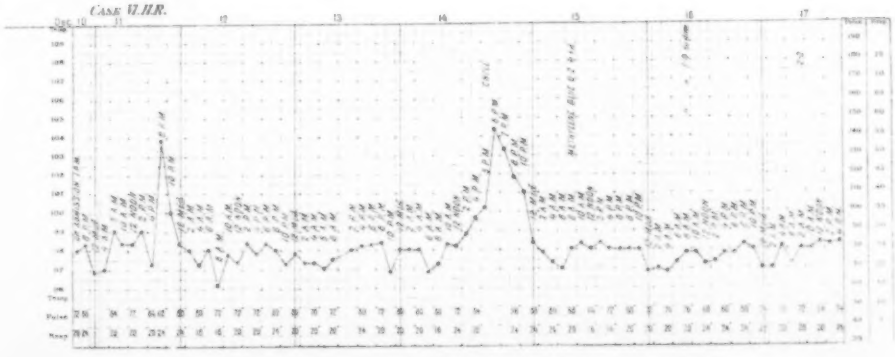
CASE III.F.R.



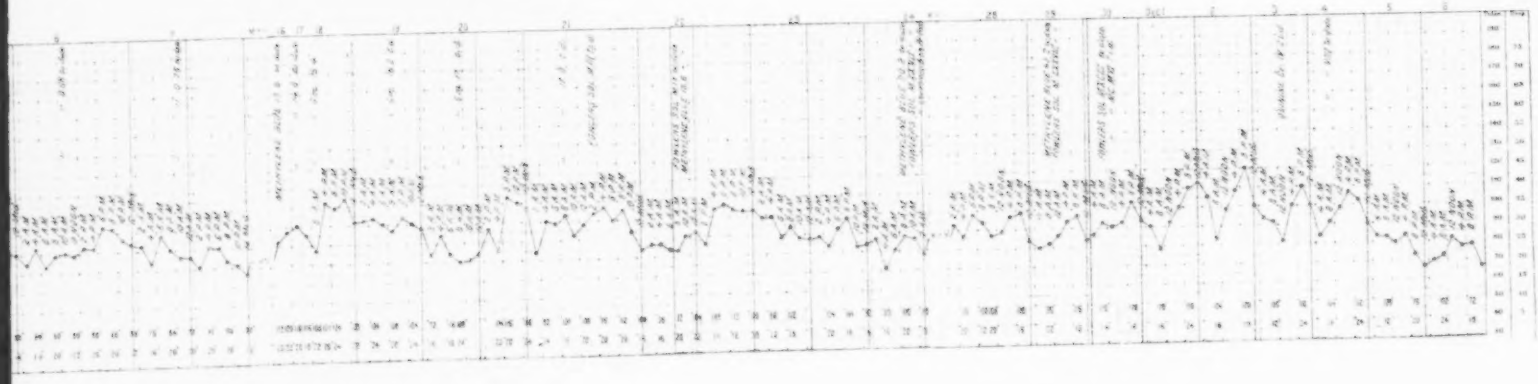
CASE V.C.W.

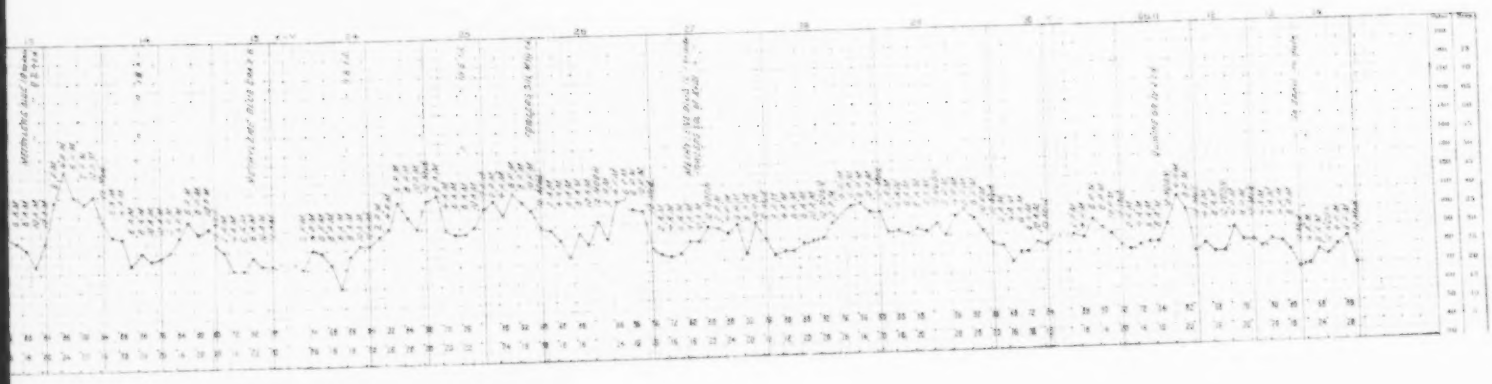


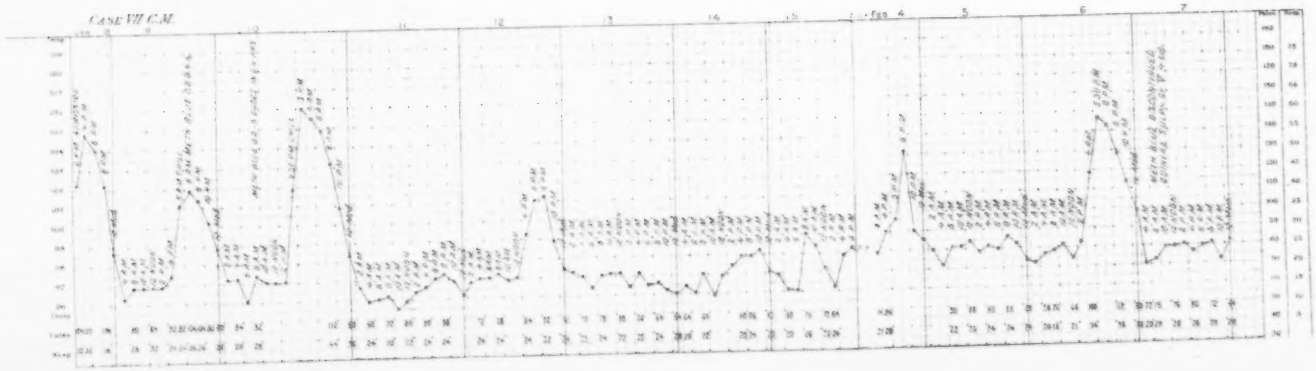
CASE VI.H.R.



TO ACCOMPANY DR. THAYER'S ARTICLE, JOHNS HOPKINS HOSPITAL BULLETIN, MAY 1892.







On the 11th there was a chill, beginning shortly after 2 P. M., temperature after the chill reaching 106° at 3 P. M. On this date very numerous segmenting bodies and fully grown organisms were seen, but a relatively small number of half-developed organisms were present in the blood.

On the 12th the temperature rose to 101° at 6 P. M., but there was no chill. From this time on until the 4th of February the temperature remained perfectly normal. The general condition of the patient was improved, but at no time was the blood entirely free from organisms. On the 4th of February, the blood not having been examined for fully a week, the patient had a slight chill, the temperature rising to 103.2°, the fall in temperature being accompanied by sweating. On the 5th the temperature remained normal, but the blood showed quite numerous, actively amœboid, pigmented, intra-cellular bodies about half filling the corpuscle, and on the 6th of February the patient had a chill, the temperature reaching 104.60° at 5.30 P. M. On the following day, the 7th, methylene-blue was discontinued, and quinine, gr. v. four times a day, was ordered. From this time on the temperature was normal and the patient felt perfectly well. During the first three or four days after the beginning of the quinine occasional organisms were seen. Unfortunately no careful examination of the blood was made during the next ten or twelve days. On the 22d careful search revealed no plasmodia. Slides examined on the 24th and 25th were also negative. On the 25th patient was discharged well. The patient went back immediately to a very malarious district and went to work in the fields. He returned on March 17th with a fresh attack of quotidian chills, with organisms exactly similar in character to those of his first entering. These have at the date of writing disappeared under quinine; no organisms were found after the fourth day.

In all these cases the *urine* while under treatment was of a deep-blue color. No albumen was present in any of the cases, excepting in Case 7, where on February 9th, two days after the omission of methylene-blue, there was a faint trace present. This was also seen two days later. No tube casts were found. No marked increase in the quantity of urine passed was noted. The *fæces* when first passed were natural in color, but on exposure to air turned rapidly blue. The *saliva* and *sweat* were not colored. In the last four cases powdered nutmeg was given with each dose of the drug, about ½ of a teaspoonful at a time, and in none of the cases was there any strangury.

The preparation of the drug was from the laboratories of Merck in Darmstadt; it was administered in capsules.

The examinations of the blood were all made with fresh unstained specimens and the Zeiss $\frac{1}{12}$ oil immersion lens, eyepieces 2 and 4.

SUMMARY.—Thus out of *seven* cases, in *two*, Case I and VI, one of tertian and one of quartan fever, a definite cure seems to have been effected. In *two* more, Cases III and IV, one a chronic case without fever but with symptoms of vertigo, and one a quotidian fever, a definite cure may have been obtained. In the former, however, it is highly probable that a more thorough examination would have revealed an occasional crescent, as the disappearance of this variety of organism is not usually so rapidly effected even with quinine; and in the second the examinations of the blood, as already noted, were not so thorough but that the rapid relapse might give rise to suspicion that organisms were still present in the blood on discharge. Of the three other cases, in *two*, Nos. II and V, which were chronic cases with hyaline bodies and crescents in the blood, an immediate temporary benefit was noted, followed later by an increase in the organisms and a return of the fever, which in the end yielded rapidly to quinine. In the other, Case VII, a quotidian, the chills disappeared rapidly and the temperature remained absolutely normal for twenty-two days, but the organisms never entirely disappeared and at the end of this time the typical tertian ague appeared again.

All of these cases were of such a nature that one might have safely expected no secondary rise of temperature after the administration of quinine, and though in the two cases in which the hyaline bodies and crescents were present the organisms might not have entirely disappeared even in one or two months, we might have been relatively certain of a speedy and entire cure in Case 7. From these observations I think the following conclusions are justified:

1. Methylene-blue has a definite action against malarial fever, accomplishing its end by destroying the specific organism; but it is materially less efficacious than quinine, failing to accomplish its purpose in many cases where quinine acts satisfactorily.

2. The action appears to be rapid, the chills disappearing or the temperature, in the remittent cases, falling to normal during the first four or five days; but later, however, if a sufficient number of organisms have resisted the drug, they appear to develop again directly under its influence, causing a return of the symptoms.

3. Methylene-blue seems to have no advantages over quinine which would warrant its further use.

NOTE.—Since the writing of this article my attention has been called to the work of Mya,[1] whose conclusions seem to agree essentially with those above expressed.

[1] Ref. British Med. Journ., March 19th, 1892.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# A CASE OF PRIMARY CARCINOMA OF THE PANCREAS WITH MULTIPLE CARCINOSIS. THE ORGANISMS OF CANCER.

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John McCready, colored, was admitted into the Johns Hopkins Hospital, in the service of Dr. Osler, on October 6th, 1891. About five weeks before his admission he was taken with a slight cough, and began to suffer from pain, especially on the left side of his chest, the pain being greatest on inspiration. At the time of his admission the cough had increased in severity and he suffered much from shortness of breath. His family history is negative. He had three brothers and four sisters still living. Beyond this nothing is known of it.

*Status Presens.*—It is observed that the patient tends to lie on the left side. He is a man of large frame and is fairly well nourished. His tongue is pale and covered with a brownish coat. Thorax:—The left side of the chest bulges outwards, and moves very little or not at all on expiration. The respirations are wheezy and 32 to the minute. On percussion the note is rather high-pitched and tympanitic throughout the right front; throughout the left front and axilla it is flat. Resonance is clear throughout the right back; flat throughout the left back. The vocal fremitus is absent over the left side. Respiration sounds at the left apex are distinct and tubular, while in the lower part of the left side they are nearly absent. The voice sounds are distinct and somewhat nasal. On the right side the voice sounds are clear, save an occasional sonorous râle. A hypodermic syringe was introduced into the left pleural cavity and some bloody fluid withdrawn. The pulse is 92 to the minute. The radial arteries are stiff, and the tension is not increased.

On October 9th the thorax was aspirated and 3500 cc. of reddish, somewhat turbid fluid were withdrawn. The patient expressed himself as much more comfortable after the aspiration, and resonance was now present to the 9th rib before, and about half-way down behind. On the 12th he was aspirated again and 1900 cc. of sanguineous fluid removed. On the 22d, 2000 cc., and on November 7th 2300 cc. more were drawn off. The morphological elements of the fluid consisted of red blood corpuscles, polynuclear leucocytes, and large polynuclear and budding cells. On November 17th the patient was transferred to the surgical ward, service of Dr. Halsted, for operation.

The operation was performed under choloform narcosis. An incision 8 cm. in length was made over the 6th rib in the axillary line and 5 cm.of the rib removed. The thickened pleura was then incised, and a brownish or reddish, slightly turbid fluid poured out in a strong stream. The patient reacted favorably. There were several small nodules in the skin upon the side of the chest which had formed about the perforations made by the introduction of the aspirating needle. One of these nodules was excised at the time of the operation and it proved upon examination to be a carcinoma. The patient died on November 18th.

The autopsy was made a short time after death by Dr. Councilman. Anatomical diagnosis: Primary carcinoma of the tail of the pancreas extending into the retroperitoneal lymph glands, then through the lymphatics of the diaphragm. Secondary carcinoma of the pleura, lungs, liver, kidney, adrenal gland, intestines and lymphatic glands. Lymphangiectasis of the pleura and small intestine.

*Exterior.*—Body of a large man somewhat emaciated. On the left side commencing 2 cm. to the left and below the nipple and following along the 6th rib, is a linear incision 8 cm. long opening directly into the pleural cavity. There are several small nodules in the skin on this side of the chest.

*Interior.*—Diaphragm on the right side at the 5th intercostal space, on the left side at the 6th rib. The left side of the diaphragm feels thick and cartilaginous. The left pleural cavity contains air and a small amount of sanguineous fluid. The right lung is much distended and does not retract. The heart is pushed to the right side and lies mostly behind the sternum. The lung is free from adhesions. Over the entire pleural surface there are lines and patches of pigment, the latter having an average size of .5 cm. In the middle of them are white areas, which are not elevated above the margins of the pigment. Along the superior border of the lower lobe there is a distinct retraction of the pleura, which is thickened here, and the thickening extends into the lung substance. At other places, between the lobes especially, are nodules of various sizes imbedded in the pleura. Many of these are very small, of grayish color, resembling somewhat the finest miliary tubercles. Others are larger, flat, with radiating masses of connective tissue going off from them and extending for a short distance over the surface.

The left lung is much reduced in volume. A few old adhesions are present, and there are several teat-like projections from the surface. The size of the lung is $14 \times 9 \times 5$cm. On section it is observed to be dense, airless, and of a leathery consistence. The pleura is much thickened over the lung and presents a red and granular appearance, and band-like processes of intensely red granulation tissue extend over the thickened pleura. The parietal pleura is thickened, the average thickness being 5 mm. It is hemorrhagic, uneven, covered with elevations and depressions, and looks fibrous. On section it is seen to be composed of grayish tissue enclosing whitish or yellowish masses. The pleural side of the pericardial sac is covered with minute nodules. The inner layers are smooth.

The liver contained a single white nodule in the interior of the right lobe. The left kidney is the seat of a yellowish nodule which occupies a renculus of the organ, having the shape of an infarction, the apex being in the pyramid. At the apex of the nodule is an occluded vessel containing a distinct reddish thrombus. The outlines of the nodule are not very sharply separated from the neighboring tissues. The right kidney contained several smaller nodules. The right adrenal gland contains a tumor mass almost filling the gland.

The pancreas contains in its tail, at a distance of 9.5 cm.

from the jejunum, a grayish tumor mass, distinctly nodular on the side next to the pancreas and measuring 6×3.5×2.5cm. It occupies the entire circumference of the organ at its seat. A second and smaller tumor mass is situated nearer the head. The retroperitoneal glands near the pancreas are enlarged and converted into grayish tumor masses, and all the glands in this situation are involved, more or less, in cicatricial tissue which extends in the form of thick radiating masses into the under surface of the diaphragm and through it, and is continuous with similar tissue on the other side.

Beneath the mucous membrane of the intestines there are a few whitish masses larger than follicles. Throughout the upper part of the small intestine there is a perfect lymph injection. The mesenteric glands are enlarged, tolerably soft, and from them a white, thin fluid can be squeezed.

Fresh frozen sections of the primary tumor and several of its metastases, including the nodules in the intestine, proved it to be a carcinoma of the glandular type. In the kidney metastasis the tumor cells contained many inclusions, readily distinguished by their bright refraction and their irregular size and form.

It is not difficult to follow the distribution of the carcinoma in this case. From the primary tumor in the tail of the pancreas the neighboring lymphatics became affected, the growth in the lymphatics then passing through the diaphragm into the left pleura. From the left pleura the right, which was far less involved, became affected, and the general infection must have taken place from the same source through the medium of the blood.

The involvement of the retroperitoneal glands and other neighboring structures in dense cicatricial tissue proceeding upwards to the under surface of the diaphragm doubtless explains the lymph injection of the intestine and the lymph congestion of the mesenteric glands. It is more than probable that the receptaculum chyli was compressed or occluded by this new growth of tissue.

The clear spaces in the pleura of the right side, which lay in the midst of collections of pigment, represented dilated lymphatic vessels filled with clear fluid. On slight magnification this was rendered perfectly evident, and the explanation is found in the obstruction offered to the passage of lymph along these channels, owing to the growth of the carcinoma within them or in their communicating branches.

We have had the opportunity of observing many instances of lymph injection of the lymphatic vessels of the peritoneal cavity and intestines. In most, if not all cases, of marked chronic passive congestion of the internal organs, whether due to lesion of the heart valves or arterio-sclerosis, which have come to autopsy here, this condition was seen. Sometimes it reached a high degree, and as there has recently appeared an account of a similar condition in the small intestine under the title "Ueber Chylangioma cavernosum" (Kruse, Virchow's Archiv, Band 125, S. 488), in which the author compares it with the cavernous angiomata, we wish to indicate this mode of their production. The mucous membrane of the intestine may show a number of circumscribed, circular, elevated bladder-like projections, sometimes having a diameter of one centimetre, which are filled with a milky fluid. They may lie between the folds of the valvulae conniventes or on the summit of them (if in the small intestine), and we have recently made a histological examination of one of the latter kind.

A piece of the intestine including the vesicle was excised and hardened in sublimate. On section the mucous membrane of the intestine was intact, but just beneath it were several lymphatic vessels much dilated, separated by very thin septa, and filled with a granular material resulting from the coagulation of the fluid contents.

The microscopical examination of the hardened tissues from the primary growth and its metastases shows the carcinoma to partake of the glandular type, and indicates its origin as having been the ducts of the pancreas. In the primary tumor the growth is not everywhere typical as regards this fact, but the pleural metastases are essentially a reproduction of duct forms. The nodules on the pleura covering the lung consist of lumina lined by a single layer of low cylindrical or cuboidal epithelial cells. There are no nodules deep in the substance of the lungs; from the surface, however, there is a slight extension of the carcinoma into the lung substance along the thickened interlobular tissue. In the primary tumor some of the epithelial cells show the same cell inclusions which have already been mentioned in connection with the fresh frozen sections of the kidney metastasis. However, as it is our intention to dwell on them at some length in treating of the latter, they can be dismissed here.

Sections made from the large wedge-shaped mass in the left kidney, in the direction of its long axis, reveal the tumor thrombus in an artery of considerable size. This thrombus does not fill the vessel entirely at the point of the sections, as there is, besides it, an organizing white thrombus present. The tumor has invaded the wall of the artery, penetrated it and passed into the parenchyma of the organ, and its ascent into the cortical portion of the kidney can be traced along the tubules. The normal epithelium of the tubules, which have been invaded by the tumor, has been displaced by the latter. Occasionally a tumor cell can be made out (apparently) in the tufts of the glomeruli in the tumor area, but they were not observed in other places. Where the tumor spreads from the vessel into the parenchyma the intertubular tissue of the organ is much thickened. In the cortex of the kidney outside the tumor area the epithelium of the convoluted tubules is much degenerated, and casts are frequently observed in the tubules.

Stained sections of the kidney afforded an excellent opportunity for the study of the cell inclusions, the so-called "coccidia" of cancer. The autopsy was a very fresh one and the tissues were preserved in alcohol and Flemming's solution, and various staining agents were employed. We did not observe new forms of inclusions, perhaps, but were able to make out many of those described by others; and in a few instances we thought that the mode of their production was perceptible. In general it may be stated that we could find but few intranuclear forms, while intracellular forms were abundant. Nuclear figures were frequently observed. Some of these were quite typical, while others were markedly irregular in form, and in still others there was a wide diffusion of the chromatin throughout the cell with only the slightest suggestion of arrangement.

We observed hyaline, refractive, more or less globular bodies devoid of stained contents lying in cells, either close by or at a distance from their nuclei. Sometimes they were perfectly homogeneous and at others granular; sometimes they were to be distinguished from the rest of the cell body only by the difference in refraction, and again they lay in distinct vacuoles. Where vacuoles occurred they varied in extent from the merest and narrowest circle to a considerable cavity, surrounding the hyaline body and presenting a double-contoured aspect. Another set of these inclusions was similar, only they contained stained particles within them, at times only one, and again several. The stained particles were not all the same size, but there was considerable variation in this respect, and oftentimes they differed from one another in shape. There was, too, a difference in refraction in the stained particles. This was not so evident in haematoxylin as it was in safranine staining. Not a few instances occurred in which these homogeneous bodies, either with or without stained particles within them, lay directly in contact with the nuclei of carcinoma cells and even compressed these greatly. We were able to observe an interesting point in connection with the formation of these bodies, inasmuch as we found, in a few instances, the remnants of a connection which had existed between the included "body" and the "host." They consisted of radially arranged fibril-like processes, very delicate but quite perceptible, which passed from one to the other. The cells of the tumor were often so closely united in the tubules that separate outlines could not be seen, and the impression of giant cell formation was obtained. In some of the large cells a considerable number of the inclusions were present, and much difference was remarked in their size and refraction, even in the same cell.

We have no difficulty in reconciling the appearances which we have described with those of many writers on the psorospermic origin of cancer and some other affections. Indeed, it is even possible to see in the variety of form and number some of the stages of development which they have depicted. We do not, however, regard these bodies as organisms, but rather interpret them as being degenerations occurring in cells and nuclei, affecting, as a rule, not the whole of these, but circumscribed portions. The observed differences in density, granulation and homogeneity may, perhaps, be accounted for on the supposition that they depend upon different degrees of one process, or represent different ages. The presence of stained particles within many of them, however, is not so easily understood in those instances where the nuclei of the cells are intact. It may be well to suggest the possibility of their being leucocytes which have wandered into the necrotic parts of cells, as leucocytes are known to enter dead cells in other cases. Some of the stained particles suggest the nuclei of polynuclear leucocytes, while in other cases it is possible to see in the irregular particles what correspond to fragments of nuclei, probably derived from those leucocytes which have perished after having entered the degenerated bodies.

The interest which the parasitic doctrine of carcinoma and some other tumor formations has provoked has suggested to us the advisability of offering a brief statement of the principal literature contributed to the subject.

In 1887 and 1888 a number of articles appeared on the ætiology of carcinoma and sarcoma, in which the authors affirmed that they had separated from these structures certain bacteria which they regarded as the cause of the respective diseases. Scheurlen[1] made a series of bacteriological examinations of primary and secondary carcinomata, and succeeded in isolating in a fair proportion of cases certain bacilli considered by him as peculiar to these growths. Rappin[2] studied five carcinomata, eight epitheliomata and three sarcomata, and separated diplococci from them. Schill[3] obtained from carcinomata, bodies which he described as polar-staining organisms, and from sarcomata similar but shorter forms. Freire[4] claimed to have first described the organisms of Scheurlen, and Francke[5] confirmed Scheurlen's observations and in addition described a bacillus which he obtained from sarcomata.

At the present time it is not considered that any one of these organisms is the cause of either sarcoma or carcinoma. The bacillus of Scheurlen is now known to be a common saprophyte, often found on the healthy skin and quite common on the nipples of healthy women and young girls.[6] The cocci of Rappin belong to the pyogenic micro-cocci, and the polar staining bodies of Schill may not be micro-organisms at all.

The theory of the parasitic origin of cancer received a new impetus in very recent times on account of the description of certain bodies, regarded as peculiar and believed to be parasitic in nature, contained within the epithelial elements of the growths. In a comparatively short space of time numerous observers have contributed the results of their investigations of this interesting subject. The study of these intra-cellular bodies has taken a wide scope, and tissues from various sources have been examined. These bodies which occupy the tissue-cells themselves, at one time the nuclei and at others the cell bodies, though some describe them as occasionally free, are not of bacterial nature. So far as any classification of them has been attempted, assuming for the moment that they are living things, they have been referred to the animal parasites, to the sporozoa.

It is stated that the first observations on the nature of these bodies were made by Neisser[7] in his contribution to Molluscum Contagiosum, but we have found that Virchow[8] described them long before and suggested the possibility of their being psorosperms. Neisser was able to study these bodies only upon microscopical sections, as culture and inoculation experiments gave negative results. He found the fresh tissues to afford the best view of the bodies, which he describes as clear and highly refractive, and he distinguishes between the spore and more highly developed stages. Neisser found them in the greatest number in the affected tissue; but he also found them in the depth of the inter-papillary processes of epithelium adjoining, in the uninjured epithelial cells.

Pfeiffer[9] described in two cases of general carcinosis and in one case of sarcoma of the breast, certain bodies which he compared to the organisms which were shown by Pasteur to be the cause of the malady of the silkworm, and he regards them as belonging to the sporozoa. Darier[10] then observed similar bodies, believed to be coccidia, in a form of cutaneous affection to which he gave the name "Psorospermose folliculaire végétante," and Darier and Wickham[11] attributed the develop-

ment of Paget's disease of the nipple to a special form of coccidia which invades the epidermis.

Malassez and Albarran[13] found certain peculiar bodies in two cases of epithelioma of the jaw which they regarded as parasites, having striking analogies with those coccidia occurring, at times, in the liver of the rabbit. Vincent [13] found similar parasitic bodies in flat-celled epitheliomata.

About this time several contributions were made which have particular interest, inasmuch as these bodies are described very fully. Thoma[14] examined carcinomata from the intestine, stomach and mamma. He found in the nuclei of the epithelial cells certain bodies, which in form, size and combinations were in such remarkable contrast to the other forms of cells as found in human beings that he considered they may well be regarded as parasites. They are unicellular bodies, 4 to 15 mm. in diameter, which are rendered more apparent by staining, and consist of protoplasm and possess nuclei and sometimes nucleoli. In form they are irregularly rounded, oftener oval; sometimes, however, they appear fusiform. In general they are quite refractive; they lie in the nuclei of epithelial cells in groups of 4 to 6, whereby the staining capacity of the nuclei is lost and these assume a hollow and bladder-like form. In other instances, immediately adjoining the nuclei, vacuoles are formed, in which similar bodies lie, or the vacuoles may contain a number of ball-like, strongly refractive objects, which may be thought of as encapsulated coccidia. Thoma does not, however, commit himself finally as to the nature of these bodies.

Sjöbring[15] endeavored to follow the life history of the supposed parasite and he describes several stages in its development. He finds a free extra-cellular form, an intra-cellular form and spore forms. He has also seen irregular forms which he thinks may indicate an active or motile stage, but he has never succeeded in observing the bodies (sarcodes) entering the nuclei of cells, although they are seen lying against and within the nuclei.

Steinhaus[16] examined a melanotic sarcoma, and the liver from a case of cirrhosis. In the sarcoma there were bodies such as other authors describe, occupying the nuclei of the cells and reaching so great a size as to reduce the original nucleus to a mere rudiment. Somewhat similar bodies occurred in the liver cells. He concedes that they may be degeneration products, but also thinks they may be parasites. Similar forms to these are, he says, described by Danilewski[17] in Polymitis malariæ, and, moreover, he regards certain forms present in his specimens as corresponding with the Karyophagus which occupies the cells of the intestine of the salamander. Later Steinhaus[18] has examined thirty cancers from different sources, in which he sometimes found the bodies and at others not; but he still considers that they may be of parasitic nature. His last communication[19] refers to an epithelioma of the plantar surface of the foot, from the study of which he concludes that the bodies described in skin cancers as foreign to them and regarded by some as parasitic, are probably not such, but are to be interpreted as hornified cells enclosed in vacuoles.

Van Heukelom[20] extended his investigations so as to include cancers of the skin, stomach, œsophagus and mamma, of the lips, mouth, intestine, rectum and kidneys, and a carcinomatous papillary cystadenoma. The metastatic growths were also examined. Those occurring in the axillary glands in carcinoma of the breast, in the liver in carcinoma of the stomach, and in the lungs following carcinoma of the stomach and pancreas. He studied nearly 200 tumors in all, and he was able to confirm the results of Sjöbring and Thoma.

Russell's[21] "fuchsin bodies" are probably closely allied to the forms already described. By means of a special and peculiar method of staining* this observer was enabled to make out certain bodies, occurring in groups of 2 to 20, which lay among the round cells at the edge of the advancing tumor, in the stroma of the cancer, and in the alveoli themselves. Out of 45 carcinomata examined he found the fuchsin bodies in 43. Yet he also observed them in a large-cell sarcoma, gumma of the dura mater, tuberculosis of the knee-joint, and in syphilis of the larynx.

On the other hand, Shattock and Ballance[22] view the "fuchsin bodies" of Russell as altered cells, and they have demonstrated them in the lung in glanders, in an unorganized thrombus of the femoral artery, a diphtheritic tonsil, and in tuberculous lymphatic glands. Piffard[23] regards the molluscum bodies as being rete cells which have undergone keratoid degeneration. Schütz[24] sees in them only altered cells, either red blood corpuscles or leucocytes, and Macallum[25] states that they may be at one time simple masses of chromatin, and at others simply leucocytes. Török and Tommasoli[26] made use of the warm chamber to determine whether or not any change and increase took place in these bodies, and they were convinced that they remained unaltered under these conditions. Transplantations from individual to individual were negative, and hens could not be infected. The effect of various caustic and injurious chemical reagents was far less marked on the molluscum bodies than on living coccidia. In this respect the former resembled colloid material, and the authors regard them as products of cell-degeneration, perhaps, not unlike this material. Klebs[27] planted pieces of carcinomata from the mamma and penis into the abdomen of white rats. Not only was he unsuccessful in causing infection of them, but the hyaline, parasite-like bodies neither increased in number nor underwent any further development. Borrel[28] has found bodies similar to those described as parasites in carcinoma, in simple inflammatory conditions of the skin, and he regards them here, as in carcinomata, as being peculiar kinds of cell degeneration and necrobiosis. Pilliet[29] examined the thymus glands of fœtuses and still-born infants at term, and found these bodies in Hassal's corpuscles. He also encountered them in the prepuce of newly-born males where agglutination to the glans existed. Moreover, he was able to make out a marked difference in the resistance of these bodies to chemical agents as compared with the coccidium oviforme as found in the liver of the rabbit. Duplay and Cazin[30] have

*The sections remain in a saturated solution of fuchsin in 2 per cent watery solution of carbolic acid for 10 minutes or longer; then they are washed in water and placed in absolute alcohol for half a minute. They are then counter-stained in a 1 per cent solution of iodine-green in 2 per cent aqueous solution of carbolic acid, where they rest for 5 minutes. Remove from this, dehydrate quickly in absolute alcohol, pass through oil and mount in balsam.

examined sixty epithelial cancers with especial reference to these supposed parasitic elements. They regarded it as an indispensable link in the chain of evidence that these bodies are of parasitic nature, that they exhibit the principal features of the evolution of the coccidia. They failed to find evidence of such changes as these organisms present, and hence they concluded that the peculiar bodies are of a degenerative character, and they consider that they result not only from cells but from mitoses. Cornil[31] and Hansemann[32] had already indicated the latter mode of origin in some cases.

Ribbert[33] made an extensive study of the cell-inclusions in carcinomata, employing for it skin and gland cancers, and, in particular, a cancer of the bladder which was especially rich in them. He used both fresh and hardened materials and a variety of staining agents. According to his investigations they are more numerous in the older than in the young portions, and the middle zone of the alveoli contains more than other parts. He looks upon the inclusions which have been described in the old literature as well as the new (see below) as degenerated and metamorphosed cells. The metamorphoses occur most commonly in those situations where the so-called "pearls," are formed. The central cell usually suffers and it becomes surrounded by 2, 3, more seldom 4 or 5 adjoining cells. Or the transformed cell may become entirely surrounded by a second, but this can only occur if the enclosed cell is smaller than enveloping one. It must be remarked in this connection that in these cases the inclusion is an apparent one only, for the included cell often occupies a depression only in the host, although in section it appears as if it were completely surrounded by protoplasm. What next happens is a reduction in volume of the enclosed cell resulting from a thickening of the protoplasm, which becomes more or less cloudy and opaque. As the surrounding cell or cells do not suffer any alteration, a vacuole is formed around the central cell. Finally the central cell loses its granular appearance, becoming more and more homogeneous, and then hyaline. The nucleus behaves in different ways. In many instances it becomes gradually more indistinct and finally fuses with the hyaline protoplasm. In others it becomes homogeneous, but shows a tendency to take coloring agents, and hence is demonstrable for a long time. The end of the process is the production of homogeneous, mostly round bodies which lie in vacuoles. They lie excentrically, or according as the section passes, nearer the center of the cell; and for the reason just stated the vacuole may, at times, appear entirely empty. As a rule, the homogeneous bodies are smaller than the epithelial cells, but they may be larger, if it happen that very large epithelial cells or giant cells suffer metamorphosis. The shape of the transformed bodies varies considerably, being round, oval or irregular. Some of the hyaline bodies contain secondary vacuoles within them, and leucocytes are found in the degenerated cells.

Another appearance is obtained when a single cell contains multiple inclusions, suggesting what Sjöbring has described as spore-cysts. On account of the number of the inclusions they could not be considered as having formed in an ordinary epithelial cell, but they must have occurred in large epithelial or giant cells. The mode of their production was not so clear, nor could it be followed as in the previous instance. These latter forms occurred in a cancer of the bladder, and they lay within the protoplasm of the cell, and, in some cases at least, represented metamorphosed nuclei of polynucleated cells. Ribbert also observed changes in karyokinetic figures which led to inclusions, and, finally, he has seen vacuoles produced by the shriveling of the nucleus, the remaining chromatin particle representing the nucleolus or simply conglutinated chromatin. Even though the process of the production of these inclusions cannot be followed in the last case as it was in the first, yet if the one is admitted to be due to cell metamorphosis, the other will not be held to have a totally different origin.

Ribbert states in conclusion that the results of the foregoing investigations, when taken together, do not permit the acceptance of the idea of the parasitic nature of the bodies included within the cell protoplasm, or lying outside of it in carcinoma, but he regards as more probable the belief that they are degenerated epithelial cells.

In a paper just presented by Kosinski[36] the author gives the results of his study of a "colloid" carcinoma of the liver secondary to a colloid carcinoma of the stomach, in which he has followed the mucoid metamorphosis of the epithelial cells. He found that the mucoid change may sometimes be very circumscribed, affecting a limited portion of the cell body or only the nucleus of the cell. Many of the appearances described by others as parasites are simulated, in his opinion, by the pictures obtained in these degenerated cells. He describes, and figures also, the presence of leucocytes in the degenerated portions of the cells. Kosinski points out that these altered tissues are markedly meta-chromatic, staining orange with safranin and violet with toluidine-blue. It is a matter of historical interest to know that some of these cell-inclusions were observed by Virchow[34] as early as 1847, although he regarded them as indicating a form of endogenous cell division. And, also, that he described in the follicles of the nail-bed similar bodies, and stated that they occurred whenever a growth of epithelium remained for a long time.[35] In conclusion we would give the titles of two reviews which have recently appeared on the subject of carcinoma, one by Stroebe,[36] "Neuere Arbeiten über Histogenese und Aetiologie des Carcinoms," the other by Cazin,[37] "La théorie parasitaire de cancer," to which we would refer for the recent literature touching other aspects of the subject than the one we have treated.

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36. Stroebe, Cent. f. Path. Anat., 1891, Nos. 10 and 11.
37. Cazin, Archiv Génér. de Médéc., 1892, p. 70.
38. Kosinski, Cent. f. Path., Band III, p. 146..

# PURULENT EPENDYMITIS, ENCEPHALITIS AND MENINGITIS WITH CONGENITAL MALFORMATION OF THE HEART AND RECTUM.

## *TOXÆMIA, BACILLUS COLI COMMUNIS FOUND IN THE TISSUES.*

BY WILLIAM T. HOWARD, JR.

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The following case occurred in the practice of Dr. L. E. Neale, of this city, to whom I am indebted for the autopsy and history. The patient was a full-term male child, three months and six days old, weighing at birth five and three-quarter pounds. Delivery was normal. The mother is a multipara, having been delivered before of two normal children.

Both parents are healthy. There is no family history of heart disease. The paternal great-grandmother and one uncle and one aunt died of phthisis. The paternal grandmother is a case of healed phthisis. The maternal grandmother died of phthisis, and one maternal aunt is said to have this disease now.

At birth the patient was feeble, small, and quite blue. As no passage from the bowels was had in two days a rectal examination was made. This revealed an imperforate rectum, the anus and sphincter ani being normal. On the third day Dr. L. M. Tiffany cut through the anus backwards, removing the coccyx, incised the posterior wall of the rectum just above the imperforate septum, and stitched the mucous membrane and skin together. During the operation the child was held by the heels; the legs, thighs and buttocks were nearly black, and the head and upper extremities were blue; its pulse and respirations were very rapid. The operation was followed by marked shock and collapse, with cyanosis lasting two days. Frequent attacks of cyanosis and collapse followed, the child having the mouth wide open, the eyes closed, and surface temperature subnormal. After the operation the stools were of normal number. The stitches pulled out and the rectal wound healed by granulation. For some weeks there was a more or less constant discharge of pus from the wound. Digital dilatation was employed daily to keep the passage open. At the sixth week there was an attack of diarrhœa and vomiting. After this the patient was dull and apathetic, for hours and days at a time, being made to take nourishment and medicines with difficulty. At the middle of the second month the child was very nervous and restless. Soon after this slight cervical opisthotonus was noticed, and occasionally flexion of the fingers and toes. These were frequent but not constant symptoms. The child rapidly lost ground, became more restless, and at times the hydrocephalic cry was heard. The scaphoid abdomen and the *tâche meningite* were not observed.

The lungs were always clear. The heart sounds were loud and clear. Congenital heart disease was naturally suspected, but no diagnosis as to its exact seat was ventured upon. The child gradually wasted away and died quietly.[1]

The following notes are taken from my autopsy records.

*Autopsy*—six hours after death.

*Anatomical diagnosis.*—Acute purulent ependymitis and encephalitis, with distension of the ventricles with pus; basic and cortical meningitis. Complete atresia of the pulmonary artery at its origin, obliteration of the cavity of the right ventricle by firm contraction, presence of but two segments at the right auriculo-ventricular orifice; patency of the foramen ovale and of the ductus arteriosus, thickening and retraction of the middle and posterior segments of the aortic valve; hypertrophy of the *right* auricle and left ventricle. Bronchitis and emphysema of both lungs and slight dilatation of the bronchial arteries. Fatty degeneration of the heart and kidneys, and fatty infiltration of the liver.

*Body.*—Wasted, small for age, 51 cm. long. There is no marked cyanosis. The cheeks are sunken, the fingers and toes somewhat clubbed. The anus is represented by a slit 5 cm., admitting the little finger with ease. The wound has completely healed. On removal of the finger a dark clot of blood follows, but no pus or fæces.

The abdomen is distended. The chest is not retracted. The aural and nasal cavities appear normal.

[1] Careful inquiry could elicit no history of a fall, or any traumatism to the head or any portion of the body.

*Head.*—The head is 34 cm. in circumference. The fontanelles are not closed. There is no evidence of a wound or contusion. On the removal of the skull-cap a few cc. of creamy pus escape on the left side. The frontal and longitudinal as well as the lateral sinuses are normal and contain fluid blood. The dura mater is removed with the skull-cap and appears normal. The pia mater over the cortex on both sides is injected, and its veins distended with blood. There is no effusion.

On the right side at the base at the under surface of the cerebellum the dura mater over the occipital bone is thickened, rough, of a dark red color, and forms one wall of a small pocket of pus.

*Cortex.*—The convolutions are somewhat flattened. At the top of the central gyrus on the right side are three or four thrombosed veins. On the same side at the parieto-occipital fissure are several small veins containing yellowish, firm thrombi. On the left side there is a more extensive thrombosis. Here the large cortical veins along the margin of the longitudinal fissure are dilated and contain firm, somewhat adherent thrombi. This thrombosis extends as far as the tip of the occipital lobe. A large one extends across the hemisphere in front of the praecentral gyrus. These thrombi are evidently old and have undergone changes, but are not purulent.

*Base.*—The condition of the fourth ventricle is remarkable. Here there is a large purulent collection, bounded posteriorly by the arachnoid. The normal appearance of the floor of the ventricle is lost. The ependyma is thickened, rough, and infiltrated with pus. The margins of the ventricle are firm. This condition of the ependyma above described extends throughout the entire floor and as far as can be seen into the iter. Above the ventricle the substance of the cerebrum is gray and infiltrated with pus. The membrane covering the under surface of the medulla and pons is red, thickened, rough, and covered with a creamy pus. The outlines of the arteries here are to be seen. The middle cerebral vessels and the pia mater in the sylvian fissure are free. There is no trace of tubercles anywhere; no lymph over the anterior perforated space, and the vessels here, when drawn out, appear normal. At the tip of the right uncinate gyrus there is a firm grayish portion of brain substance, which on section opens into a large purulent cavity, through the middle (descending) cornu of the right lateral ventricle. The same condition is observed on the left side. At the apex of the cornu the ependyma is exceedingly firm.

On section the brain substance is very soft and œdematous. On opening the lateral ventricles they are evidently dilated and distended with a creamy, gelatinous, yellowish green pus. The posterior cornua are dilated and their walls softened. There is a large collection of pus in each anterior cornu.

The choroid plexuses are firm and hard, with evident thickening of the membrane covering them. The structures of the third ventricle are extensively softened and the venæ Galeni are distended with soft clots. The lateral walls of this, like those of the other ventricles, are softened, the ependyma thickened, soft, deeply congested, with uniform hemorrhagic infiltration in places.

At the upper surface of the right lateral ventricle, at the junction of the middle and anterior cornua, there is beneath the ependyma a grayish yellow mass which on section proves to be a pocket of pus in the brain substance. Part of the wall of this is firm and hard. On the other side, above and almost in a corresponding position, there is beneath the ependyma a still larger purulent collection, the size of a walnut. Its thick and firm walls are 2 mm. in thickness, and consist of an inner grayish opaque purulent layer and an outer translucent layer.

The medulla and pons are hyperæmic, but contain no purulent foci; the membrane covering them is red, injected and thickened. The crura show only congestion. The portion of the cord seen through the foramen magnum is soft and œdematous, and the membranes covering it are hyperæmic. Careful search reveals no tubercles anywhere.

*Abdomen.*—Peritoneum smooth, pale. A small amount of pale straw-colored fluid in its cavity. The surface of the intestines is very pale. There are no adhesions.

*Heart.*—The peri- and epi-cardia are smooth, pale, no effusion. The wall of the right ventricle is strongly contracted. The right auricle is dilated and hypertrophied, the fossa ovalis is deep, the foramen ovale patent, measuring 12 mm. in diameter. The left ventricle is relatively large, globular in shape, its walls hypertrophied, and the myocardium firm. The left auricle is dilated and hypertrophied. The pulmonary orifice is completely closed, the foramen ovale and the ductus arteriosus are both patent. The weight of the heart is 31 grams.[1]

*Lungs.*—Are pale, distended with air at anterior margins, where there is some emphysema. There is some atelectasis of the posterior portions. Muco-pus is squeezed out of the bronchi. The pleural cavities are normal.

*Liver.*—Small, measuring 10×7×2.5 cm. It is of a dark red color on the surface. The edges are round. The cut surface is of a pale grayish-yellow color. The lobules are visible, the consistency is normal. The bile duct is free. The gall bladder contains a slightly viscid pale yellow bile.

*Spleen.*—Not enlarged, of a dark reddish-brown color. The cut surface appears normal.

*Kidneys.*—The right kidney is a little larger than the left. Both kidneys are of the same general appearance. Both are lobulated. The capsules are easily removed. On section they are pale, the striations visible. The average width of the cortex is 4 mm. The right kidney measures 5×2.5×2 cm.

*Pancreas.*—Normal. Suprarenal bodies normal.

The stomach, duodenum and small intestine are pale. There are no ulcerations. They contain a small amount of yellow mucus. The colon, cæcum and vermiform appendix are normal.

Four cm. above the anal orifice there is a distinct raised constriction 3 cm. in circumference, corresponding to the point where the rectum was incised. This appears as a band of white fibrous tissue. The wound is entirely healed, and there are no ulcers or abrasions. The mucous membrane of the rectum above the constriction is soft, slightly red, and thrown into folds. That portion below the constriction is pale white, and measures 2.5 cm. in circumference. The anal sphincter is well preserved.

[1] The description of the heart is reported at length in The Archives of Pediatrics for January, 1892.

Microscopical examination of frozen sections of the wall of the left ventricle of the heart shows a slight amount of fatty degeneration. There is intense fatty infiltration of the liver cells, and fatty degeneration of the epithelial cells of the tubules of the kidneys.

Microscopical examination of hardened sections of the wall of the lateral ventricles shows an entire loss of the epithelial cells forming the ependyma. The wall resembles in many respects an abscess wall of any other part. Throughout the greater part, the ependyma and a portion of the brain substance underlying it are in a state of coagulation necrosis. This part stains homogeneously with eosine. Beneath this there is an area of infiltration with polynuclear leucocytes. The ependyma is entirely destroyed.

Sections cut through the walls of the ventricles and taking in the deep portions of the brain substance show small foci of abscess formation. These foci show a central coagulation necrosis with a more or less wide surrounding area of polynuclear cell infiltration.[1] These areas are especially numerous in the tissues beneath the floor of right lateral ventricle. They are also seen in sections made from the cortex cerebri, just above and in front of the anterior cornu of the right lateral ventricle. These areas of encephalitis or minute abscess formation of the brain tissue are probably secondary to the ependymitis which is the starting-point of the changes.

The membrane covering the medulla and pons is thickened, with a fibrous exudation containing polynuclear leucocytes. There are no tubercles to be seen anywhere. No bacteria are to be found in the tissues.

Sections from the roots of the lungs show a slight dilatation of the bronchial arteries. The pulmonary vessels are of normal size. The bronchi, large and small, have lost some of their epithelia, and their walls are here and there infiltrated with polynuclear leucocytes, and their lumina contain desquamated epithelial cells, leucocytes, a few red-blood corpuscles, and granular detritus. There is well marked emphysema, and here and there areas of atelectasis. The liver and kidneys show nothing worthy of note.

Sections through the junction of anus and rectum show complete union.

*Bacteriological Examination.*—Cover-slip preparations of the pus from the ventricles and of the pus from the base of the brain show the presence of two varieties of bacteria, (1) a small micrococcus and (2) a short, stout bacillus. Both of these forms are present in considerable numbers.

*Agar.*—Agar and gelatine roll cultures were made from the pus of the lateral ventricles and from the liver and right kidney. In the tubes from each of these sources there were numerous colonies of the same kind, which on cover-slip preparations were composed of a short bacillus. This organism, after testing its manner of growth on agar, gelatine, potato, and in litmus milk and in bouillon, was found to be indistinguishable from the bacillus coli communis, except that it possesses active motility.

Lately Prof. Welch in his studies on the bacillus coli communis has obtained from the fæces of healthy persons and from cultures made at autopsies many specimens of typical colon bacilli which possess active motility.

This bacillus stains readily with the aniline dyes and is decolorized by the Gram method.

The micrococcus seen on the original cover-slip preparations did not grow in the culture tubes and was therefore in all probability dead. This result would suggest that the process was of some date, as it is well known that the staphylococcus pyogenes and the streptococcus pyogenes and other pyogenic bacteria often fail to grow in cultures made from old abscesses. The organism was not in the form of a diplococcus and had no capsule.

The variety and rarity of the lesions found in this case stamp it as a remarkable one. The condition of the heart has been fully discussed elsewhere.

Since the writings of Rilliet in 1846 a non-tubercular inflammation of the brain and its meninges in children has been clearly recognized both clinically and pathologically by authors, but not until recent years has its relative frequency been appreciated.

According to Rilliet, it is only in very young children with simple meningitis that fluid is found in the ventricles, but it is now generally agreed that a fluid, serous or purulent, is not uncommonly present in the ventricles in this form of inflammation, and that in a certain proportion of cases the ependyma and the choroid plexuses show signs of inflammation.

Netter has been the chief worker on the bacteriology of simple meningitis. Out of a series of twenty-five cases examined by him and recorded in 1889, the diplococcus pneumoniæ was present in fifteen, the streptococcus pyogenes in four, an intracellular diplococcus in two; a short active bacillus, the bacillus of Friedländer, and a slender, small bacillus, respectively, in the remaining three cases.

Monti has reported four cases in which the diplococcus pneumoniæ was present.

The fact that meningitis is so often secondary to pneumonia and otitis media goes far to explain the great frequency with which the pneumococcus is found as the cause of the lesion.

On the other hand the streptococcus is the cause of most of the sequelæ of rheumatism and the various zymotic diseases which meningitis not uncommonly follows.

In the present case the original focus of infection was an unusual one, a suppurating rectal wound. We take it that the coccus found in the pus of the ventricles and of the meninges was the cause of the ependymitis and the encephalitis, and that the general infection with the bacillus coli communis occurred from the same source but at a later period.

Escherich (Fortschritte der Medicin, 1885, No. 15 u. 16) and others, and later, Welch and Blachstein (Johns Hopkins Hospital Bulletin, July, 1891), have produced acute infection in rabbits and guinea-pigs by subcutaneous and intravenous injections of this organism.

Blachstein describes an acute, a subacute, and a chronic infection of rabbits following intravenous injections of the bacillus coli communis.

The injection of 1.5 cc. of a twenty-four hour old bouillon culture of the organism found in my case into the peritoneal

[1] There is no increase in the capillaries, but those seen appear dilated.

cavity of two guinea-pigs was followed by death in from eight to ten hours. In each case there was found at autopsy acute fibrino-serous peritonitis, pleuritis and pericarditis. The organism was obtained in pure culture in these cases in large numbers from the exudate of all of these cavities, and from the blood, liver, lungs, spleen, and kidneys.

Though it has been demonstrated by Welch and others that the bacillus coli communis is alone present in many cases of inflammation of various portions of the body, in this case the inflammatory lesions were produced by a mixed infection with the micrococcus found in the pus from the brain and the bacillus coli communis.

A strong exciting cause was the very feeble circulation in the brain allowed by the congenital malformation of the heart.

We would sum up the interesting features of the case as follows:

1. Purulent ependymitis, meningitis and encephalitis.
2. The presence in the inflammatory area of a micrococcus and the bacillus coli communis.
3. Congenital atresia of the pulmonary orifice, patency of the foramen ovale and of the ductus arteriosus, and persistence of the fœtal circulation.
4. Congenital imperforate rectum.
5. The association of congenital malformation of the heart and rectum, a suppurating rectal wound, and inflammation of the ependyma, brain and meninges.

## OBITUARY.—D. MEREDITH REESE, M. D.

At the close of the meeting of the Historical Club, upon April 11th, Dr. Welch took the chair and announced the death of Dr. D. Meredith Reese, a former Assistant Resident Physician at the Johns Hopkins Hospital, which had occurred at Saranac Lake, N. Y., that morning, and made appropriate remarks. Remarks were also made by Drs. Kelly, Brush, of the Sheppard Asylum, Lafleur, Thayer, Finney and Hurd. Drs. Finney, Thayer and Hewetson, as a committee appointed to prepare resolutions expressive of the feeling of the associates of Dr. Reese, made the following report, which was unanimously adopted:

WHEREAS, it has pleased Almighty God to take from us our beloved friend and former associate, D. MEREDITH REESE, M. D.

*Resolved*, That the members of the staff of the Johns Hopkins Hospital do hereby express their sincere sorrow at the untimely closing of a life which gave promise of great achievements.

*Resolved*, That in his death we have lost a true and cherished friend, and the medical profession a talented and enthusiastic member.

*Resolved*, That the staff do also express their great sympathy with the widowed mother and bereaved family, and that a copy of these resolutions be forwarded to his family, and that they be published in THE BULLETIN OF THE JOHNS HOPKINS HOSPITAL and in *The Maryland Medical and Surgical Journal*.

# PROCEEDINGS OF SOCIETIES.

## THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

*Meeting, January 4th, 1892.*

DR. HALSTED in the chair. 30 members present.

**Foreign Bodies in the Ear.**—DR. THEOBALD.

Dr. Theobald exhibited a number of foreign bodies removed from the ear and made observations upon the same. He first pointed out the importance of being sure that a foreign body is in the ear before attempts are made to remove it, as much harm is often done through mistakes of this character. The popular belief is that the presence of a foreign body in the ear must, necessarily, give rise to serious consequences, and hence that its immediate removal is imperative. This belief is almost groundless. If the foreign body be inanimate, it will, probably, produce no immediate ill effects, unless it be of an irritant character or be so wedged in the auditory canal as to cause mechanical irritation by pressure upon its walls or upon the tympanal membrane. Hasty attempts by unskillful persons, with unsuitable appliances, to remove such bodies are, therefore, to be deprecated, as usually they result in more harm than would ensue from the undisturbed presence of the foreign body. In most instances, especially in the hands of persons not in the habit of operating upon the ear, the syringe is the most useful agent for the removal of foreign bodies from the auditory canal. No harm can ensue from its use, and generally it accomplishes the desired result. As a rule, forceps cannot be used advantageously for this purpose, because, in the narrow canal, the blades cannot be opened wide enough to grasp the intruding body. Occasionally, however, the shape of the latter is such that it may be grasped by a slight separation of the blades, and under such circumstances forceps answer very well. A blunt traction hook, with the under surface of the hooked extremity serrated and having the handle set at an angle of about one hundred degrees with the stem, is the instrument which Dr. Theobald has found most useful for the removal of such bodies as cannot be brought out by means of the syringe. Even if the body be tightly wedged in the canal, the point of the hook can be insinuated beyond it and the body dragged or rolled out. During all such manœuvres the ear must be illuminated by reflected light, and every movement of the instrument watched. In difficult cases, displacement of the auricle and cartilaginous meatus has been recommended to facilitate the extraction of the foreign body. He had never met with a case in which such a procedure seemed indicated, and he did not think he would ever find it necessary to resort to it. Live insects entering the ear may cause great suffering through the movements of their wings and claws. Any bland oil poured into the ear will kill them, and thus give immediate relief. Maggots are occasionally deposited in the auditory canal, especially when a purulent discharge is present, and as they are apt to attach themselves to the canal wall they may cause great suffering. They are hard to kill, and may require to be dragged from their point of attachment with forceps. Among the foreign bodies exhibited was a tick, which was found attached

to the meatus wall and had to be removed in this manner. The most difficult foreign substance to remove from the ear which Dr. Theobald had encountered, was a mass of cerate that an indiscreet physician had melted and poured into the meatus in order to destroy an insect which had penetrated there. The end he had in view was accomplished, but, as may be imagined, the remedy proved worse than the disease.

## RESIDENTS' ASSOCIATION.

The second annual dinner of the Residents' Association of the Johns Hopkins Hospital occurred May 5th, 1892, in the Residents' Parlor. The President, Dr. Hunter Robb, occupied the position of toast-master. The following toasts were responded to: "The Speaker of the Evening," Dr. Osler; "The Johns Hopkins Hospital," Dr. Hurd; "The Evolution of Gynæcology," Dr. Kelly; "The Historian," Dr. F. R. Smith.

The following members of the Association were present: Drs. G. H. F. Nutall, W. S. Thayer, J. Hewetson, F. R. Smith. W. T. Councilman, H. Phippen, J. M. T. Finney, A. C. Abbott, L. F. Barker, E. M. Parker, T. S. Cullen, W. W. Russell, A. L. Stavely, J. G. Clark, A. Hoch, E. Van Ness, S. Flexner, A. L. Ghriskey.

Invited guests: Drs. Osler, Hurd, Kelly and Lotsy.

## NOTES ON NEW BOOKS.

Anleitung zur Aseptischen Wundbehandlung. Dr. C. SCHIMMELBUSCH, Assistenzarzt der Königl. Chirurgischen Universitätsklinik des Geh.-Rath v. Bergmann in Berlin. (*Berlin*, 1892, *August Hirschwald.*) A manual, 12mo of 200 pages, with a short preface by Dr. E. von Bergmann, and with 28 illustrations in the text.

This little book cannot fail to do good, and we commend it to every practitioner and student of surgery. The author considers his subject under the following heads:

1. The significance of the aseptic treatment of wounds.
2. Air and contact infection.
3. The causes of wound infection.
4. Disinfectants.
5. Disinfection of the surface of the body.
6. Sterilization of metal instruments.
7. Aseptic dressings.
8. Aseptic sutures and ligatures.
9. Aseptic wound drainage.
10. Aseptic materials for sponges.
11. Aseptic injection and puncture.
12. Aseptic employment of catheters and bougies.
13. Fluids for cleansing and irrigation.
14. Wards and operating rooms.
15. Aseptic operations and wound treatment.
16. Aseptic emergency dressings and the treatment of injuries.
17. Bibliography.

One would not expect to find much that is new in such a book as this; but in chapter 6 which treats of the sterilization of metal instruments the author advocates a method which originated with him and which he described about nine months ago in Langenbeck's Archives. The instruments are boiled for five minutes or less in a 1 per cent. solution of washing soda. The soda prevents the rusting of the instruments and increases very much the sterilizing power of hot water.

Behring discovered to his astonishment that the ordinary soda lye of the laundry at a temperature of 85° C. killed anthrax spores often in four minutes and always in eight or ten minutes. The usual concentration of the washing lye is 1.4 per cent.

In the author's experiments staphylococci and the bacillus pyocyanius were killed in the boiling 1 per cent. soda solution in two to three seconds, and anthrax spores which in several instances had resisted steam at 100° C. were killed in two minutes. A dipping of the instruments for several seconds would, according to S., suffice to kill the pyogenic organisms, and a boiling for five minutes in the soda solution should satisfy all the claims of ordinary practice.

Rapidity and certainty of germ destruction are not the only advantages of the author's method. Of great worth is the simplicity of its accomplishment. One requires nothing more than may be found in any household,—fire, water, washing soda and a vessel.

The author has devised for v. Bergmann's klinik an apparatus in which to boil the instruments. It provides for rapid heating of the water and convenient transfer of the instruments. Illustrations, though not very good, facilitate the description of the apparatus. The instruments having been sterilized are transferred to trays containing carbol-soda solution (aa 1 per cent.) or preferably to a boiled soda solution (1 per cent.)

Accepting Schimmelbusch and Behring's experimental results we have boiled our instruments in the 1 per cent. soda solution ever since the publication of Schimmelbusch's article about nine months ago. This method has a disadvantage which Schimmelbusch does not mention. The instruments are so slippery when removed from the soda solution that, for us at least, it is practically impossible to work with them. We have been obliged, therefore, to discard the use of the carbol-soda solution (aa 1 per cent.) for the instrument trays, and return to the carbolic acid solution (1–30). The instruments having been boiled in the 1 per cent. soda solution are thoroughly rinsed in 1–30 solution of carbolic acid before being placed in the instrument trays.

In chapter 7, p. 104, Schimmelbusch informs his readers that catgut is made from the sheep's intestine and not, as the name would indicate, from the intestine of the cat. He describes the manufacture of catgut as follows:

"In accordance with Lister's directions, the small intestine of the sheep is freed of its mesentery, washed in water, and then manipulated upon a board with an instrument like the back of a knife. As the blunt instrument is drawn with a scraping motion over the intestine the so-called 'dirt' is removed; this is nothing else than the mucous membrane of the intestine. In like manner the circular muscular coat is rubbed off, so that only the very thin tube constituted by the longitudinal muscular coat remains, which may be inflated so as to represent a well preserved delicate tube-like structure. From this the threads are manufactured by twisting, and according to the thickness desired either the entire tube or strips of the same are employed."

To suppose catgut to be made from the longitudinal muscular coat of the intestine might be an excusable error if a knowledge of the gross anatomy of the wall of the intestine were not indispensable to every surgeon. To attempt, for instance, a circular suture of the intestine without any knowledge whatever of the coats of the intestine is, to say the least, not right. No one familiar with the coats of the intestine would for a moment accept the suggestion that catgut is made from the longitudinal muscular coat, or believe that this coat could be so dissected as to represent a perfect tube which might be distended with air. Catgut is made from the submucosa and not from the longitudinal muscular coat. The submucosa[1] is the most important coat of the intestine for the surgeon. Without it a circular suture of the intestine would be an almost certainly fatal operation.[2] The submucosa may be readily disengaged from the other coats of the intestine by simply engaging the intestine firmly between the handles of a scissors and pulling the intestine. The handles allow nothing but the submucous coat

[1] Halsted: Circular Suture of the Intestine. American Journal of Medical Sciences, October, 1887. Halsted: Intestinal Anastomosis. Johns Hopkins Hospital Bulletin, No. 10, January, 1891.

[2] Kummer's operation (*vid.* Archiv für Klin. Chirurgie, 1891, Bd. XLII, Heft 4), is a badly conceived one. I have tested it four times on dogs. All of the dogs died sooner or later from perforation. The muscular "cuffs" unsupported by the submucosa expand into the thinnest conceivable film and finally rupture.

to pass between them. The serous and muscular coats become stripped off from the outer side and the mucous coat from the inner side of the intestine. The submucosa may then be inflated and dried. From the submucosa obtained in this way we have made what we call gut-wool. We use this gut-wool solely for the purpose of stopping excessive hemorrhage from bone. To manufacture the gut-wool the dried submucosa is moistened with absolute alcohol and cut into fine shreds with a tobacco-cutting machine. The wool is then preserved in an alcoholic solution of corrosive sublimate (1–1000.) To plug bone sutures or bleeding points in bone take a very small quantity of the wool in a sharp-pointed forceps and press it into the bone. We have found this to be an instantaneous and infallible method of arresting hemorrhage in bone.

Chapter 15, on aseptic operating and the aseptic treatment of wounds, disappoints us. Schimmelbusch entertains v. Bergmann's great dread of blood in wounds, and upholds the assertion made ten years ago by the latter, that no surgeon should look for good results who does not with the greatest care stop every bleeding point. Our work alone,[1] clinical and experimental, has taught us not to fear a dead space occupied, without tension, by a blood clot more than an obliterated dead space whose walls, constricted by obliteration sutures, are studded with ligatures and little areas of strangulated tissue. The rapidity with which granulation tissue fills a dead space is marvelous, provided the circulation of the walls of the dead space be vigorous and has not been interfered with by ligatures or sutures. A cavity as large as an English walnut in the cancellous tissue of bone, for example, may become completely filled with granulation tissue in forty-eight hours. Whether antiseptic precautions be employed or not, the blood clots, occupying freshly made dead spaces, become, as a rule, promptly "organized," and very rarely break down, even when they have been inoculated with pyogenic micro-organisms.[2] In only one instance did an inoculated blood clot break down.

The drainage tube is of necessity a part of the technique of those who insist upon perfectly dry wounds. It would be illogical for them to close absolutely their wounds, for the dead spaces which necessarily exist in almost every wound must become filled with something, either blood or transudate, and this fluid something is according to the advocates of this method a thing to be feared and gotten rid of. The dead space may be exceedingly small, but what is true for the large must, in a measure, be true for the small dead spaces, and one can hardly conceive of a dead space too small to lodge bacteria and to contain food for them. But one cannot attempt to drain minute dead spaces nor, perhaps, any but large ones. How then can the believers in the absolutely dry method explain their own good results?

The objections to the insertion of drainage tubes into wounds have been well summed up by Welch,[3] as follows:

*First*, they tend to remove bacteria which may get into a wound from the bactericidal influence of the tissues and animal juices. *Second*, bacteria may travel by continuous growth or in other ways down the sides of a drainage tube and so penetrate into a wound which they otherwise would not enter. We have repeatedly been able to demonstrate this mode of entrance into a wound of the white staphylococcus found so commonly in the epidermis. The danger of leaving any part of a drainage tube exposed to the air is too evident to require mention. *Third*, the changing of dressing necessitated by the presence of drainage tubes increases in proportion to its frequency the chances of accidental infection. *Fourth*, the drainage tube keeps asunder tissues which might otherwise immediately unite. *Fifth*, its presence as a foreign body is an irritant and increases exudation. *Sixth*, the withdrawal of tubes left any considerable time in wounds breaks up forming granulations and thus both prolongs the process of repair and opens the way for infection. Granulation tissue is an obstacle to the invasion of pathogenic bacteria from the surface, as has been proven by experiment. *Seventh*, after removal of the tube there is left a tract prone to suppurate and often slow in healing.

The first and second objections are, I believe, original with Dr. Welch. I would add an *eighth* objection. Tissues which have been exposed to the drainage tube are suffering from an insult which impairs more or less their vitality and hence their ability to destroy or inhibit micro-organisms. W. S. Halsted.

[1] Johns Hopkins Hospital, Vol. 2, No. 5. Surgical fasc.

[2] Experiments on the so-called organization of the blood clot by Dr. Welch, Dr. W. T. Howard, Jr., and myself in the Pathological Laboratory of the Johns Hopkins University and Hospital, *vid.* Welch: Conditions underlying the Infection of Wounds, Am. Journ. of the Medical Sciences, Nov., 1891.

[3] Some Considerations concerning Antiseptic Surgery. Maryland Medical Journal, Nov. 14th, 1891.

Consumption: How to prevent it and how to live with it. Its nature, its causes, its prevention, and the mode of life, climate, exercise, food, clothing necessary for its cure. By N. S. Davis, Jr., A. M., M. D. (*Philadelphia and London, F. A. Davis*, 1891.)

The author's intention is to present certain rigid sanitary rules for the guidance of consumptives and practitioners of medicine who have to deal with them. He speaks of the nature of consumption, and very properly of its causative agent, the bacillus tuberculosis of Koch, and of the causes which favor its development within the body, and afterwards of the prevention of consumption by the destruction of sputa, proper residence, pure air, climate and systematic physical training. The remainder of the book is taken up with the hygiene of the consumptive and the treatment of consumption. The intention of the book is excellent and the work is in the main well done. The directions for the disinfection of sputum are good, and the remarks upon climate are judicious—as also those upon medical treatment. There are, however, several omissions which, if supplied, would add to the value of the book. The action of the bronchial glands in disposing of dust and other injurious foreign bodies is not mentioned. The germicidal action of blood serum is also not mentioned. The Adirondacks, probably the best resort in America for consumptives, are not mentioned. The book is disfigured by mistakes in grammar and spelling which seem inexcusable, as *e. g.* "*matterate*," p. 8, for suppurate; Chester, *Michigan*, for *Illinois*; oose for *ooze*, p. 21; "woolen-ware" for *woolen-wear*; Hyeras for *Hyères*, etc. Sentences like the following are common: "Furnace and stove heat *is* not the most desirable," "Frequent changes from the care of one physician to another *is* detrimental." That an author who attaches A. M. to his name should be guilty of such schoolboy errors suggests a fresh inquiry as to the value of degrees on the part of the American Academy of Medicine. H.

The Nurse. A monthly journal devoted to the interests of Nurses and the Sick. Edited by Annie E. Parker. (*The Boston Medical and Sanitary Bureau, Boston.*)

We are glad to see another Nursing Journal added to the few already in existence and to notice that it promises to be of decided practical value to nurses. Its articles and extracts are concise and instructive. It discusses hygiene, therapeutics, dietetics and practical points in nursing. We question, however, the necessity or advisability of establishing a "Medicine Chest" for nurses, as it is generally understood and taught that prescribing medicines is out of her province and that they are only administered by her under medical direction.

This magazine can be made of great interest to all engaged in nursing. I. A. H.

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